Amendments to the Specification:

Please replace the paragraphs starting at page 4, line 19 and ending at page 4, line 31 with the following amended paragraphs:

Thus, it is an object of the present invention, to provide a pharmaceutical composition of small-sized, sucrose liposomes for a parenteral administration of an active compound, which comprises: (i) liposomes with an average diameter of about 75 nm to about 300 nm, wherein the unilamellar membrane is formed by a mixture of saturated lipids containing a ratio of lysophospholipids of about ~~0,5~~ 0.5 mol% to about ~~6,0~~ 6.0 mol% of the total lipids content, and (ii) ~~an encapsulated~~ a therapeutic compound ~~contained in~~ being encapsulated inside said liposomes.

Preferred concentrations of lysophospholipids are those of about ~~1,4~~ 1.4 mol% and about ~~2,8~~ 2.8 mol% regarding the total lipid content.

Please replace the paragraphs starting at page 6, line 20 and ending at page 6, line 31 with the following amended paragraphs:

The lipids used for the preparation of the unilamellar membrane are saturated lipids, preferably selected among phosphatidylcholine, cholesterol and phosphatidyl ethanolamine, phosphatidylinositol, phosphatidylglycerol, natural phosphatidylcholine (from soybean and/or eggs) and hydrogenated phosphatidylcholine obtained from different natural sources like soybean or eggs, distearoyl fosfatidylethanolamine derivatized with polyethyleneglycol 750-5000, preferably, polyethyleneglycol 2000 - O-methylated and/or glycolipids like GM1 or other sialogangliosides, dipalmitoyl phosphatidylethanolamine derivatized with O-methylated polyethyleneglycol 750- 5000 or combinations thereof.

Please replace the paragraphs starting at page 7, line 14 and ending at page 7, line 23 with the following amended paragraphs:

According to the present invention, liposomes of small size are obtained by the addition of lysophospholipids to the lipid mixture that will conform the liposomal membrane, preferably with a content of lysophospholipid which varies between about ~~0,5~~ 0.5 mol% and

about ~~6,0~~ 6.0 mol% related to the total amount of lipid content. Most preferably, the content of lysophospholipids could be from about ~~1,4~~ 1.4 mol% to about ~~2,8~~ 2.8 mol%, related to the total amount of lipid content.

Please replace the paragraph starting at page 8, line 3 and ending at page 8, line 22 with the following amended paragraph:

Preferably, the lipid mixture is dissolved in an organic solvent which is evaporated up to dryness. The lipidic membrane formed is taken up with an aqueous solution, the suspension being subjected to 3 and 6 freezing cycles (from about -20°C to -45°C) and unfreezing (up to 50°C – 60°C). Afterwards, the suspension is extruded through polycarbonate membranes [Preparation of liposomes of defined size distribution by extrusion through polycarbonate membranes, by Olson F., Hunt, C.A., Szoka, F.C., Vail, W.J., Papahadjopoulos, D., Biochem. Biophys. Acta, 557, 9-23 (1979); Vesicles of variable size produced by a rapid extrusion procedure, by Mayer, L.D., Hope, M.J., Cullis, P.R.; Biochem. Biophys. Acta 858, 161-168 (1986)]. In the present invention, extrusion starts with the membrane of biggest pore, e.g. 1000 nm, followed by a membrane of smaller pore (400 nm) and following with membranes of the smallest pore size (50 nm), until liposomes of the desired size are obtained.

Please replace the paragraph starting at page 9, line 7 and ending at page 9, line 18 with the following amended paragraph:

In another embodiment of the invention, it was found essential, for the supply of therapeutically effective doses of a variety of cytotoxic agents, to load the liposomes with high concentration of the active principle. For example, for cytotoxic agents such as anthracyclinic antibiotics, particularly anthracyclinic antibiotics such as doxorubicin, epirubicin, daunorubicin, salts thereof and similar compounds, it is desirable to obtain a ratio of encapsulated active principle of about ~~8,5%~~ 8.5% w/w to about 11.5% w/w referred to the weight of the lipid content of the liposomes.

Please replace the paragraph starting at page 10, line 2 and ending at page 10, line 12 with the following amended paragraph:

Particularly preferred starting calcium ions solutions are calcium chloride solutions at a concentration from about 50 mM to about 200 mM. Other soluble salts of calcium may be used. pH Buffering components, when they are used, shall not include sequestrating calcium substances. Acetic/acetate solutions as well as any other anion solution which do not produce calcium ion precipitation may be used. An aminoacid, such as histidine, could also be used. The ratio of liposome solution to calcium chloride solution may be of about ~~1,5~~ 1.5 to 0.05 – ~~0,5~~ 1.5 (v/v).

Please replace the paragraph starting at page 11, line 3 and ending at page 11, line 8 with the following amended paragraph:

The mixture is evaporated in a rotatory evaporator up to dryness, trying not to exceed a temperature of 45°C. The formed film is taken up in an ammonium sulfate solution at 45°C (5 ml of a solution containing about ~~13,2~~ 13.2 mg/l), with stirring at room temperature.

Please replace the paragraphs starting at page 11, line 22 and ending at page 11, line 35 with the following amended paragraphs:

A solution containing 95 mg of hydrogenated soybean phosphatidylcholine, ~~1,5~~ 1.5 mg of palmitoyl lysophosphatidyl choline, 30 mg of phosphatidyl ethanolamine derivatized with O-methyl polyethileneglycol-2000 and 30 mg of cholesterol in 15 ml of anhydrous ethanol is prepared.

The mixture is evaporated in a rotatory evaporator up to dryness, at a temperature not higher than 45°C. The film formed is taken up in a solution of ammonium sulfate at 45°C (5 ml of a solution containing ~~13,20~~ 13.20 mg/l)under stirring at room temperature. The liposomes obtained in the previous step are submitted to freezing (-45°C) and thawing (50°C) cycles. At least 6 cycles are performed.

Please replace the paragraph starting at page 12, line 5 and ending at page 12, line 7 with the following amended paragraph:

The average size of liposomes in this preparation is shown in Figure 1 with an empty circle (~~1,43~~ 1.43 mol% of lysophospholipid/ total lipids.)

Please replace the paragraph starting at page 12, line 15 and ending at page 12, line 19 with the following amended paragraph:

The mixture is evaporated in a rotatory evaporator until dryness, at a temperature not higher than 45°C. The formed film is taken up in a solution of ammonium sulfate at 45°C (5 ml of solution containing ~~13,20~~ 13.20 mg/l), under stirring at room temperature.

Please replace the paragraph starting at page 13, line 2 and ending at page 13, line 7 with the following amended paragraph:

The mixture is evaporated in a rotatory evaporator up to dryness, trying to perform it at a temperature not higher than 45°C. The formed film is taken up in solution of ammonium sulfate at 45°C (5 ml of solution containing ~~13,20~~ 13.20 mg/l), with stirring at room temperature.

Please replace the paragraph starting at page 13, line 15 and ending at page 13, line 17 with the following amended paragraph:

The average size of liposomes in this preparation is shown in Figure 1 with a void triangle (~~11,5~~ 11.5 mol% of lysophospholipid /total lipids).

Please replace the paragraph starting at page 13, line 25 and ending at page 13, line 29 with the following amended paragraph:

The mixture is evaporated in a rotating evaporator up to dryness, at a temperature not higher than 45°C. The film formed is taken up in solution of ammonium sulfate at 45°C (5 ml of a solution containing ~~13,20~~ 13.20 mg/l), with stirring at room temperature.

Please replace the paragraph starting at page 14, line 2 and ending at page 14, line 4 with the following amended paragraph:

The average size of the liposomes in this preparation is shown in Figure 1 with a

full square (~~14,3~~ 14.3 mol% of lysophospholipid / total lipids).

Please replace Table 1with the following amended Table 1:

Example No.	**Lyso PC content in mol%** (Lyso PC/Total lipids)	Size measured of liposomes containing progressive quantities of Lyso PC after extrusion through membrane of 400 nm
Control	---	310 nm
1	~~1,43~~ 1.43	215 nm
2	2.86	240 nm
3	~~11,5~~ 11.5	208 nm
4	~~14,3~~ 14.3	75 nm

Please replace the paragraph starting at page 15 line 6 and ending at page 15, line 12 with the following amended paragraph:

Afterwards, a solution containing the following composition is prepared: ~~1,5~~ 1.5 volumes of liposomes in suspension, 1 volume of a doxorubicin hydrochloride solution containing 6 mg/ml of said compound in a sucrose solution 10% (w/v) and histidine ~~0,15%~~ 0.15% (w/v) and ~~0,5~~ 0.5 ml of a solution of sucrose 10% /histidine ~~0,15%~~ 0.15 (w/v) (buffer sucrose/histidine).

Please replace the paragraph starting at page 15 line 15 and ending at page 15, line 26 with the following amended paragraph:

The degree of encapsulated doxorubicin hydrochloride is determined by UV spectrometry (absorbancy at 590 nm). With this purpose, absorbancy determinations on samples of liposomes with encapsulated doxorubicin dilutions in alkaline isotonic medium (free of doxorubicin) and on samples of liposome with encapsulated doxorubicine dilutions in alkaline medium containing detergent (total doxorubicin) are performed. Through the

absorbancy data obtained at 590 nm the percentage of encapsulation of ~~78,7%~~ 78.8% is calculated. The percentage of free doxorubicin is ~~21,3%~~ 21.3%.

Please replace the paragraph starting at page 15 line 31 and ending at page 15, line 35 with the following amended paragraph:

~~1,5~~ 1.5 volumes of liposomes suspension, ~~0,4~~ 0.4 volumes of sucrose/histidine buffer (according to example 5), ~~0,1~~ 0.1 volumes of solution 100 mM of Cl_2Ca and ~~1,0~~ 1.0 volume of doxorubicin hydrochloride solution, 6 mg/ml in sucrose /histidine buffer.

Please replace the paragraph starting at page 16 line 3 and ending at page 16, line 8 with the following amended paragraph:

The percentage of doxorubicin incorporated is determined (as depicted in example 5), obtaining a value of ~~87,9%~~87.9%. The percentage of free doxorubicin is ~~12,1%~~ 12.1%. As can be seen, the degree of incorporation is ~~9,2~~ 9.2 points higher than the one obtained without Cl_2Ca.

Please replace the paragraph starting at page 16 line 14 and ending at page 16, line 15 with the following amended paragraph:

The percentage of encapsulation of doxorubicin hydrochloride is ~~91,2%~~ 91.2%.

Please replace the paragraph starting at page 16 line 20 and ending at page 16, line 24 with the following amended paragraph:

The percentage of encapsulated doxorubicine is ~~95,53%~~ 95.53, e.g. ~~4,33~~ 4.33 points higher than without the adding of calcium chloride. In other words, the percentage of free doxorubicin is 50% less than without the addition of calcium chloride.

Please replace the abstract with the following amended paragraph:

A pharmaceutical composition of small sized unilamellar liposomes for the supply active principles by injection, with an improved permanency in the blood flow, where the unilamellar membrane contains a mixture of saturated lipids encompassing at least one

lysophospholipid in a quantity from about 0.5 mol% to about ~~6,0~~ 6.0 mol% with reference total lipids and the production method. Additionally, liposomes of high encapsulation efficiency of an active principle like doxorubicine are prepared through the adding of a solution of calcium ions.